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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/056,908	01/25/2002	Christopher A. Hinkel	TM0141-UT	2363
22847	7590	11/03/2005		
SYNGENTA BIOTECHNOLOGY, INC. PATENT DEPARTMENT 3054 CORNWALLIS ROAD P.O. BOX 12257 RESEARCH TRIANGLE PARK, NC 27709-2257			EXAMINER SWITZER, JULIET CAROLINE	
			ART UNIT 1634	PAPER NUMBER

DATE MAILED: 11/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action  
Before the Filing of an Appeal Brief**

Application No.

10/056,908

Applicant(s)

HINKEL ET AL.

Examiner

Juliet C. Switzer

Art Unit

1634

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 14 July 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☐ The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.  
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**NOTICE OF APPEAL**

2. ☒ The Notice of Appeal was filed on 14 July 2005. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

**AMENDMENTS**

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
(a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);  
(b) ☐ They raise the issue of new matter (see NOTE below);  
(c) ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
(d) ☒ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See Continuation Sheet. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
5. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.  
6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
The status of the claim(s) is (or will be) as follows:  
Claim(s) allowed: \_\_\_\_\_.  
Claim(s) objected to: \_\_\_\_\_.  
Claim(s) rejected: 13-17, 19, 20, 25-31.  
Claim(s) withdrawn from consideration: \_\_\_\_\_.

**AFFIDAVIT OR OTHER EVIDENCE**

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

**REQUEST FOR RECONSIDERATION/OTHER**

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See Continuation Sheet.  
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). \_\_\_\_\_.  
13. ☐ Other: \_\_\_\_\_.

  
**JULIET C. SWITZER**  
**PRIMARY EXAMINER**

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Continuation of 3. NOTE: The amendment adds claim 36 and does not cancel any other claim. This claim requires further search and examination, and thus the amendment does not materially reduce or simplify the issues for appeal.

Continuation of 11. does NOT place the application in condition for allowance because: Regarding the rejection under Lai et al. in view of Fulton et al., applicant argues that there is no motivation to combine the references, beginning at page 7 of the response. Regarding the motivation, as discussed in the rejection, Fulton et al. specifically teach that the use of microbeads and flow cytometry detection have a wide range of applications. To that end, at page 1750 of the reference, second column, Fulton et al. give guidance as to how to apply the use of microbeads to a wide variety of target molecules, including oligonucleotides. At p. 1755, Fulton further expand their discussion of the benefits and wide applicability of their system teaching that "the system has several advantages for analysis of biologically and medically relevant molecules, including speed, economy, and advanced analytical capabilities..." and further specifically suggest the use of the system for capture/sandwich assays, which is precisely the type of system that Lai et al. are using. The examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, specific motivation has been cited in the rejection, and this specific motivation is found in the teachings of Fulton et al. At page 8 of the response, application states that "one of skill would have to engage in considerable experimentation in order to reconcile the two teachings" and that there is no reasonable expectation of success if the two teachings were combined. However, these are attorney's arguments which are not supported by any evidence on the record, and which Fulton et al.'s teachings of the broad applicability of their method seem to contradict. As previously discussed, Fulton et al. are very clear in their suggestion that their methods using microspheres and flow cytometry have wide applicability to a variety of different binding assays, specifically mentioning oligonucleotide binding and capture assays. Absolute predictability is not required in order to establish an expectation of success. The MPEP states, "Obviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness (2143.02)." However, in the instant case, no evidence is presented, only the arguments of counsel. The arguments of counsel are not found to be persuasive in the absence of a factual showing. MPEP 716.01(c) makes clear that "The arguments of counsel cannot take the place of evidence in the record. In *re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant." Applicant sets forth further explanation beginning in the second paragraph on page 9, outlining the differences in the microspheres used by Lai et al. versus Fulton et al., and suggesting that in view of the differences, there would have been no valid motivation to combine the references. However, this is not persuasive, because one could have used the microbeads and detection method as taught by Fulton et al. As noted, applicant provides no evidentiary support for the assertion that there is no reasonable expectation of success. The rejection is maintained.

The arguments regarding Lai et al. in view of Fulton et al. and further in view of Wallace et al. rely on the previous arguments regarding Lai et al. in view of Fulton et al. and are not persuasive for the same reasons.

Applicant traverses the rejection under the '611 patent in view of Gerry et al. and further in view of Fulton et al. beginning at page 10 of the response. Applicants argue that Gerry et al. does not provide for the deficiencies of the '611 patent because Gerry et al. does not teach or suggest a capture probe coupled to a microbead. This is a piecemeal analysis that does not consider the totality of the rejection, and thus it is not persuasive. Applicant further argues that Fulton et al. do not teach how to obtain the desired result when coupled with the disclosures of the '611 patent and Gerry et al. This is not persuasive. As noted in the rejection, Fulton et al. utilize capture probes attached to microbeads and detection via flow cytometry. Fulton et al. teach methods of sorting and detecting microspheres which utilize flow cytometry, and in particular teach these methods in conjunction with nucleic acid hybridization methodologies (p. 1753-1755). Fulton et al. teach the multiplexed assays which utilize the microspheres are suitable for use with oligonucleotide target molecule (p. 1750), and teach that with respect to hybridization assays that the no-wash format of many microsphere-based assays, particularly in the final detection step, is considerably faster than assays that require multiple washings (p. 1755). They also teach that the rapid kinetics of microsphere-based assays that allow shorter incubation times than conventional solid supports (p. 1755). Thus, the teachings of Fulton et al. are more than a suggestion to investigate, the specifically exemplify how to use the microbeads in nucleic acid based detection systems. The rejection is maintained.

Applicant traverses the rejection under Chen et al. in view of Dubiley et al., stating that there is no motivation to combine the references (see p. 14 of the response). In support of this argument, applicants discuss the differences in methodology between Chen et al. and Dubiley et al. suggesting that the methods are not combinable. However, this is not persuasive. Dubiley et al. are relied upon to provide teaching of a particular type of sets of primers; Chen et al. provide all of the other elements of the claims. Applicant's analysis of the two methods does not take in consideration the totality of the rejection which describes the necessary modification to Chen et al. or the motivation given to modify the method taught by Chen et al. in order to have arrived at the claimed invention. Applicant states that Chen et al. would not have been motivated to utilize the solid phase assays taught by Dubiley et al. as the methods of Chen et al. were more amenable to multiplexing. The examiner has not argued that one would be motivated to use the solid phase assay of Dubiley et al., but instead to have modified the primers taught by Chen et al. so as to have used those taught by Dubiley et al., and such a modification would have been motivated in order to provide an alternate methodology for the detection of single nucleotide polymorphisms using the basic methodology taught by Chen et al., as Dubiley et al. teach that the use of primers that end adjacent to or overlap with the polymorphic site have comparable specificity with regard to one another (final page, first full paragraph). The use of the method for the detection of disease alleles would provide the obvious benefit of detecting disease alleles and thus the presence or predisposition to disease.

The traversal of the rejection under Chen et al. in view of Dubiley et al. and further in view of Soderlund et al. and the traversal of the rejection of Lai et al. in view of Fulton et al. and Wallace et al. and further in view of Soderlund et al. rely on the previously set forth arguments which have been addressed in both the Final rejection and this Advisory rejection. As the previously set forth arguments were not persuasive, the rejections are maintained.

Applicant's traverse the rejection under Huang et al. in view of Fulton et al. pointing out differences in the two methods and that there would be no motivation to combine the references. The motivation is provided in the rejection. Applicant's arguments that the "sweeping statements" by Fulton et al. do not provide sufficient motivation are not persuasive. As noted previously, Fulton et al. exemplify their method in nucleic acid based assays and very clearly suggest the broad applicability of their methodology. Applicant has provide no evidence that their guidance would not be sufficient.

Thus, all rejections are maintained.